

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of :
MUMPER ET AL. : Confirmation No.: 5127
Serial No.: 10/072,320 : Group Art Unit: 1618
Filed: Feb. 7, 2002 : Examiner: Rogers, James W.
For: Ph-SENSITIVE MUCOADHESIVE FILM-FORMING GELS AND WAX-FILM COMPOSITES
SUITABLE FOR TOPICAL AND MUCOSAL DELIVERY OF MOLECULES

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is a Pre-Appeal Brief Request for Review of the final rejections made in the Office Action mailed on January 14, 2011, submitted concurrently with a timely Notice of Appeal and fee. Upon carefully considering the following comments and arguments of record incorporated herein by reference, the Applicant believes the panel will find that the Examiner has committed factual and legal errors in rejecting the claims. The claims stand variously rejected as allegedly obvious over U.S. Patent Nos. 6,270,783 to Slavtcheff et al. ("Slavtcheff"), 4,715,369 to Suzuki et al. ("Suzuki"), and 6,562,363 to Mantelle et al. ("Mantelle").

First, the Applicant's prior arguments have consistently been misinterpreted. The Applicants have never argued that the cited references do not list certain compositions similar to those set forth in the Applicant's disclosure. Rather, the Applicants contend that there is no reason articulated for the skilled artisan to combine any of the ingredients listed in the references to provide the claimed pH-sensitive mucoadhesive compositions, and likewise that the requisite expectation of success of arriving at the claimed compositions is lacking. Further, the Applicants contend that the rejections lack support because certain alleged teachings of the relied-on references are couched as trademarks rather than as specific compositions having known properties. For example, in the 8-16-2010 Action (*pg 5*, bottom ¶) the Examiner stated (in reference to the trademark Carbomer®) that "[T]he same compound is the same no matter what the name is given to the compound." *Contra* this statement, rather than identifying any specific polymer the trademarks referenced in at least Slavtcheff and Mantelle are associated with product lines comprising a number of products formulated to provide a wide range of disparate chemical properties. Therefore, simply reciting the trademark cannot, without more, provide a rational reason leading the skilled artisan to make combinations providing specific properties such as the claimed pH-sensitive mucoadhesive compositions having the claimed properties.

The mere recitation of known building blocks for the presently claimed compositions, without more, does not

provide the required guidance leading the skilled artisan to consider the present claim limitations of pH-sensitivity and mucoadherence. To use an overly simplistic analogy, under the law on obviousness a document describing rivets and another document describing steel girders cannot, without more, render obvious a claim to a suspension bridge. In the present case, the skilled artisan reading the relied-on references is not faced with a finite number of identified, predictable solutions affording a reasonable expectation of success, or an objective reason leading inevitably to a finding of *prima facie* obviousness of claims directed to a pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester. Rather, the skilled artisan is provided only a lengthy list of ingredients, some provided only as trademarks that cannot without more identify specific compositions with specifically defined properties, with no reason articulated for the skilled artisan to consider any particular combination thereof to arrive at the presently claimed subject matter other than the guidance provided by the present specification.

Turning now to the rejection of claims over Slavtcheff and Suzuki, Suzuki is cited solely for teachings of thin layers for adhesive patches and for use of a wax backing layer. Slavtcheff is cited for teachings of various compositions, including methacrylic acid, Carbomer®, and others. Nowhere does Slavtcheff teach or even hint at use of *mucoadhesive* polymers, much less the presently claimed *pH-sensitive* anionic mucoadhesive polymers, for delivery of a molecule of interest to mucosa as a function of pH. Thus, it cannot fairly be said that the combination of Slavtcheff and Suzuki articulates any reason for the skilled artisan to consider the precisely claimed pH-sensitive anionic mucoadhesive copolymers of the present independent claims. It is believed that the panel will agree that, particularly in the chemical arts, mixing of even the same compositions in different proportions and/or under different conditions can result in polymers having very distinct chemical properties. For that reason, it is believed that even if the panel finds that Slavtcheff/Suzuki teach or suggest each and every element of the present independent claims as is required to support *prima facie* obviousness, the panel will agree that the references articulate no reason for combining the elements to provide compositions having properties as presently claimed, and by failing to provide that reason likewise fail to provide the requisite expectation of success that remains a necessary element of *prima facie* obviousness.

The Examiner points to nothing in Slavtcheff/Suzuki believed to lead the skilled artisan to contemplate providing an adhesive having pH-sensitive mucoadhesive properties as expressly claimed. Slavtcheff teaches only a temperature-sensitive skin-adhesive layer (*Col. 3, ll 1-4*) comprising liquid crystal thermochromic substances (*Col. 2, ll 25-65*) and a water-interactive agent inducing a temperature change (*Col. 2, ll 15-17*) causing the thermochromic substances to change color indicating that the adhesive has dried sufficiently to adhere keratotic plugs (*Col. 5, ll 18-24*). There is simply no indication in Slavtcheff of any need or reason for pH-sensitivity or mucoadherence. The rejection therefore appears to be based solely on Slavtcheff's naked recital of various known ingredients, including monomers such as methacrylic acid (*Col. 4, ll 51-54*), Carbomer® (*Col. 5, ll 15-17*), and others (see *Col. 5* and *Col. 6*). Absent undue experimentation or use of the present specification as a blueprint, Slavtcheff/Suzuki provide no teaching or reason for the skilled artisan to consider combining compositions to achieve a pH-sensitive mucoadhesive layer comprising at least one water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive mucoadhesive polymer, for delivering a molecule of interest to mucosa. Rather, at most Slavtcheff/Suzuki provide

motivation to consider combinations of compositions formulating an adhesive for adhering to skin and having thermochromic properties, with no motive provided for the skilled artisan to consider any requirement for pH sensitivity or mucoadherence. Failing to provide such reason, the combination of Slavtcheff/Suzuki likewise cannot provide a reasonable expectation of success of the claimed subject matter, and therefore fails to establish *prima facie* obviousness of the independent claims.

The argument supporting the failure to establish *prima facie* obviousness of the claims over Slavtcheff/Suzuki applies equally to the rejection of claims over Slavtcheff in view of Suzuki, further in view of Mantelle. Slavtcheff and Suzuki are cited for the propositions addressed above. Mantelle is cited for a teaching of use of Noveon® and Eudragit® polymers in adhesive compositions for “personal use” (see the 10-9-2009 Office Action at *pg* 6, second full ¶). Slavtcheff/Suzuki provide no teaching or reason for the skilled artisan to contemplate the presently claimed combinations, nor does the art provide any reasonable expectation of success of the combinations. In turn, inclusion in the analysis of Mantelle’s acknowledgment of the known product line of Noveon® and Eudragit® polymers does not adequately support *prima facie* obviousness.

As set forth in the Response filed on Nov. 3, 2010 (*pg* 15, third full ¶), the trademarks Noveon® and Eudragit® are applied to a wide range of different polymers having an equally wide range of different properties, and thus Mantelle’s mere recitation of trademarks does not and cannot rise to the level of a teaching or rationale sufficient to motivate the skilled artisan to combining any teachings of Slavtcheff, Suzuki, and Mantelle to arrive at a pH-sensitive mucoadhesive layer as precisely set forth in the present independent claims. Supporting this proposition, certain claims of the application were previously rejected as indefinite (see the 8-16-2010 Action, at *pg* 3) because of recitations of those trade names/trademarks, under the rationale that “... the trademark or trade name cannot be used properly to identify any particular material or product” If a trademark is so vague that its inclusion renders a claim indefinite, then in turn surely a mere mention of the trademark without more cannot motivate the skilled artisan to combine particular compositions branded under that trademark to arrive at a chemical composition having specific chemical properties. At the least, it is believed to be a fair statement that the advocated combination of Slavtcheff/Suzuki/Mantelle provides no reason leading the skilled artisan to arrive at the present pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and an anionic pH-sensitive film-forming polymer as claimed, and likewise offers no reasonable expectation of success. At most, what is provided is an open invitation to experiment.

Further, the only guidance offered by Mantelle expressly leads the skilled artisan away from pH-sensitive polymers. Mantelle at *Col. 38, ll 1-6* recites particular acrylic adhesives believed to be suitable, including Eudragit®. However, Mantelle expressly teaches use of only Eudragit® RL and RS. As previously demonstrated (see the Response filed on Feb. 8, 2010, at *pg* 13, and Exhibit 1 appended thereto), the trademarks Eudragit® RL and RS are associated with polymers whose swelling properties are pH-insensitive. Thus, to the extent that Mantelle leads the skilled artisan to consider a Eudragit® polymer, it is to a pH-*insensitive* polymer that the skilled artisan is led, not the diametrically opposed pH-*sensitive* film-forming polymers as claimed.

Even more, Mantelle leads the skilled artisan towards a preferred combination of neutral polymers and another bioadhesive (see at least Mantelle *Col. 4, ll 65 et seq.*: “... the inventors believe that the combination of PVP and

another bioadhesive provides for a superior adhesion not attainable by either the PVP or another bioadhesive alone.”). As set forth in the Response filed on Aug. 3, 2009, at pg 12 first full ¶, PVP and/or ethyl cellulose as taught by Mantelle are known to be neutral polymers. Thus, Mantelle would not motivate the skilled artisan to consider anionic adhesive polymers without PVP, but rather guides the skilled artisan toward inclusion of the neutral polymer. In contrast, the present independent claims recite anionic polymers, and at least the Applicant’s independent claims 67 and 68 expressly exclude non-anionic polymers. For at least these reasons, Slavtcheff/Suzuki/Mantelle cannot support *prima facie* obviousness of the independent claims.

The argument supporting the failure to establish *prima facie* obviousness of the claims over Slavtcheff/Suzuki/Mantelle applies equally to the rejection over Mantelle in view of Suzuki, in that it is believed that no combination of Mantelle/Suzuki articulates any reason for the skilled artisan to contemplate the presently claimed combinations of a pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer of polyacrylic acid cross-linked with polyalkenyl ether or divinyl glycol and an anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester.

The lengthy teaching of ingredients (including trademarks) set forth in Mantelle combined with the wax backing taught by Suzuki does not, without more, provide a basis for an obviousness rejection of the present independent despite any recent revisions to the Manual of Patent Examining Procedure. Rather, some articulated reason for combining those teachings is needed. For the reasons stated above, Mantelle’s mere recitation of trademarks cannot rise to the level of a teaching or articulated reason sufficient to motivate the skilled artisan to consider combining the teachings of Mantelle and Suzuki to arrive at a pH-sensitive mucoadhesive layer as recited in the pending independent claims. Further, to the extent Mantelle provides any motivation to the skilled artisan, it is to select pH-insensitive and neutral adhesive polymers. The rejections should be reversed.

Prima facie obviousness of a claim is established only when the prior art and/or the knowledge available to the skilled artisan teach or suggest each and every limitation of the claim, as well as articulating some reason the skilled artisan would consider the combination,¹ not “merely by demonstrating that each of [the claim] elements was, independently, known in the prior art.”² A rejection of claims as obvious combinations of prior art elements also requires articulating a finding that the results flowing from the combination would have been predictable to the skilled artisan. Thus, even if the references taught each and every one of the limitations of the present independent claims, as

¹ *In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993); *In re Bell*, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993); Manual of Patent Examining Procedure §2143; *In re Wada and Murphy, citing CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) and *In re Royka*, 490 F.2d 981, 985 (CCPA 1974); *Takeda Chemical Industries Ltd. v. Alphapharm Pty.*, 83 USPQ2d 1169 (Fed. Cir. 2007) (quoting *KSR Int’l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1731 (2007)).

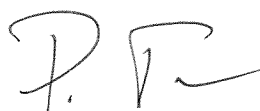
² *KSR Int’l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727 (2007); Examination Guidelines Update: Developments in the Obviousness Inquiry after *KSR v. Teleflex*, Fed. Reg. Vol. 75, No. 169, Sept. 1, 2010, citing *Crocs, Inc. v International Trade Commission*, 598 F.3d 1294 (Fed. Cir. 2010); Manual of Patent Examining Procedure §2143 A(3). To reject a claim as *prima facie* obvious based on features disclosed in one or more references, there must be some suggestion, either in the art itself or in the knowledge available to the skilled artisan, of the desirability of making the combination (Manual of Patent Examining Procedure ch. 2100, Section 2143.01, p. 131: “The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.”) (Emphasis in original). Still further, it is required that a reasonable expectation of success support the finding of obviousness. *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

recently emphasized³ to the examining corps the law dictates that this alone does not establish *prima facie* obviousness without a rational, articulated reason for combining reference teachings. Although an “obvious to try” rationale can support a rejection under 35 U.S.C. §103 under certain narrowly defined circumstances,⁴ this only applies when there are a “finite number of identified, *predictable* solutions, *with a reasonable expectation of success*” (emphasis added), and the requirement for providing an objective reason leading the skilled artisan to combine references remains.⁵

Independent claims 33, 66, 67, and 68 require combinations of compositions including at least a pH-sensitive mucoadhesive layer comprising a water-insoluble swellable anionic mucoadhesive polymer and at least one anionic pH-sensitive film-forming copolymer of methacrylic acid and acrylic or methacrylic ester, for delivering a molecule of interest to mucosa. No reasonable interpretation of the cited art teaches or suggests each of these limitations, articulates any reason for combining teachings of the references to provide pH-sensitive mucoadhesive polymers according to the claims, or affords any reasonable expectation of success of the combinations. For at least these reasons, *prima facie* obviousness of the independent claims is not established, and the claims are in condition for allowance over the cited art. The claims depending therefrom are likewise in condition for allowance without consideration of obviousness.⁶

Upon careful review and consideration, it is believed the panel will agree that the Applicants have identified factual and legal errors that would lead to a reversal of all the present rejections on Appeal and that all the pending claims are patentable over the cited prior art. Therefore, the panel is respectfully requested to remand the application to the Examiner with instructions to withdraw the Section 103 rejections of the pending claims. The Commissioner is authorized to charge fees and credit overpayments to the undersigned representative’s **Deposit Account 11-0978**.

Respectfully submitted,
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³ Examination Guidelines Update: Developments in the Obviousness Inquiry after KSR v. Teleflex; Fed. Reg. Vol. 75, No. 169, Wed., Sept. 1, 2010, pp. 53643-53660, at 53647, citing *Crocs, Inc. v. U.S. International Trade Commission*, 598 F.3d 1294 (Fed. Cir. 2010).

⁴ See, Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.*, Fed. Reg. 72, No. 195, 57526-57535, at pg. 57529.

⁵ *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories, Inc. and Mylan Pharmaceuticals, Inc.*, (2007-1223 (Fed. Cir. 2008) (“... the passage in KSR posits a situation with a finite, and in the context of the art, small or easily traversed, number of options that would convince an ordinarily skilled artisan of obviousness.”); see also *Takeda Chemical Industries Ltd. v. Alphapharm Pty.*, 83 USPQ2d 1169 (Fed. Cir. 2007).

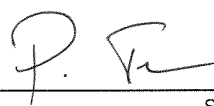
⁶ *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) (“[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious”); *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

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PTO/SB/33 (07-09)

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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) 434-400 DIV	
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		First Named Inventor Russell Mumper	
		Art Unit 1618	Examiner Rogers, James W.
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <div style="display: flex; justify-content: space-between;"><div style="width: 45%;"><p>I am the</p><p><input type="checkbox"/> applicant/inventor.</p><p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p><p><input type="checkbox"/> attorney or agent of record. Registration number _____</p><p><input checked="" type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 <u>55,684</u></p></div><div style="width: 50%; text-align: center;"><div style="margin-bottom: 10px;"> _____ Signature Patrick M. Torre _____ Typed or printed name (859) 252-0889 _____ Telephone number <u>3-14-2011</u> _____ Date</div></div></div> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p>			
<p><input checked="" type="checkbox"/> *Total of <u>1</u> forms are submitted.</p>			

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